In addition, as suggested by the Examiner, the claim no longer recites the term "new" and uses the term "compound" in place of "compounds".

Claims 1-11 were rejected under 35 U.S.C. 103 as being unpatentable over U.S. Patent 4,328,334 to Kobrehel, et al. Kobrehel, et al. fail to suggest or render obvious the present invention since the R_1 group suggested by Kobrehel, et al. does not encompass a methyl group as required by the present invention. Instead, R_2 according to Kobrehel, et al., can be hydrogen, an alkanoyl, or a 4-R-Ph-SO_2 group. However, it has been found, according to the present invention, that the presence of the N-methyl group provides compounds which have improved activity, and/or toxicity, and/or stability as compared to the compounds disclosed by Kobrehel, et al. Along these lines, attached hereto are Tables 3-6 which represent testing of compounds of the present invention and comparison of such to erythromycin A. Along these lines, the testing of the antibacterial activity on a number of gram-positive and gram-negative clinical isolates (see Tables 3 and 4) showed a substantially higher sensitivity of the tested strains against N-methyl-11-aza-10-deoxo-10-dihydro erythromycin A in comparison with erythromycin A, and at the same time, the number of the resistant microorganisms was diminished in a high degree.

Furthermore, the determination of the acute toxicity on NMRI mice, according to the Litchfield-Wilcoxon method showed that the N-methyl-11-aza-10-deoxo-10-dihydro erythromycin A is less toxic than erythromycin A (see Table 5).

The testing of the stability of the compounds of the present invention in acidic medium showed that the N-methyl-11-aza-10-deoxo-10-dihydro erythromycin A and the 13,14-cyclic carbonate thereof possess at a pH, of 1.2 (condition simulating the condition in the gastro-intestinal tract), a higher stability than erythromycin A (see Table 6). The stability testing was carried out by exposing the tested compounds to the action of 1N HCl

during 30 minutes, 1,3, and 6 hours, as well as the determination of minimal inhibitory concentrations with the use of the test strain staphyloccoccus aureus ATCC 6538T. The above tests will be presented in the form of a verified showing, if so desired by the Examiner.

In conclusion, it is believed that each of the claims in this application is definite and clear. It is further believed that the reasons why the present invention distinguishes over the prior art have been fully set forth. Reconsideration and allowance are therefore respectfully solicited. If the Examiner thinks that an interview might serve to advance the prosecution of this case in any way, the undersigned attorney is available at the telephone number noted below.

Respectfully submitted,

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TABLE 3

The antibacterial activity on gram-positive clinical test microorganisms

Test strain	Compound	MIC (mcg/ml)										
		0.5	1.0	2.0	4.0	8.0	16.0	32.0	64.0	128.0	R	No.
ENTERO-COCCUS	E	26	11	9		6	3		1		7	63
	1	15	13	10	6				4			
STAPH. AUREUS	E	9	7	12							13	41
	1	11	10	4	6	3					7	
STAPH. ALBUS	E	22	6	12		2						42
	1	30	12									
STREPTO-COCCUS PNEUMON.	E	9	7									16
	1	11	5									
STREPTO-COCCUS HAE-MOLYTICUS	E	17	3									20
	1	13	7									
No.	E	83	34	33		8	3		1		20	182
	1	80	47	14	12	3			4		12	182

E - Erythromycin A

1 - N-methyl-11-aza-10-deoxo-10-dihydroerythromycin A

TABLE 4

	1					4	4	–				
KLEBSIELLA AEROGENES	E							1		2	7	1
	1						9		1			
PROTEUS MIRABILIS	E						3				3	1
	1					1	2	1	10		2	
PSEUDOMONAS AERUG.	E									1	9	
	1						1		1	5	3	
ENTEROBACTER AEROG.	E									1	17	1
	1					3	6	6	2		1	
ENTEROBACTER LIQUEF.	E							1				
	1					1						
MIMA POLYMORPHA	E							1			2	
	1								2	1		
HERELLA	E						1	3	1	1		
	1			1	1			3	1			
HAEMOPHYLUS INFLU.	E		1		2	3						
	1		3	3								
NO.	E		1	0	2	3	16	35	45	15	64	17
	1		3	8	43	54	28	13	17	7	6	17

E - Erythromycin A

1 - N-methyl-11-aza-10-deoxo-10-dihydroerythromycin A

TABLE 5

The acute toxicity (mg/kg)

Compound[+]		LD_{50}	LD_{16}	LD_{84}
Erythromycin A	I.V.	360(241.9)[++]	280	460
	I.P.	520(349.4)	326	840
	P.O.	-	-	-
Compound of Example 1	I.V.	825(421.6)	610	1020
	I.P.	1200(513.2)	1010	1400
	P.O.	>10000(5100)		

[+]The compounds were tested in the form of their lactobionate salts.

[++]The results are calculated on the contents of the active component.

TABLE 6

The stability in acidic medium

Exposition time (h)	MIC (mcg/ml)		
	Erythromycin A	Compound of Example 1	Compound of Example 7
Controll	0.1	0.1	0.5
0	5	0.1	0.5
1/2	10	0.1	0.5
1	10	0.5	0.5
3	25	1.0	1.0
6	25	2.5	1.0

Strain: Stapylococcus aureus ATCC 6538-P